Analysis of Carcinogenic Potential in Female Mouse Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: March 7, 1997 (14:52) Source: c:\amouse\xrod.txt

아이들이 시작 시원 사용 등 시하다는 어떻게 된 생활하를 하는 것이다.

Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)
For missing Tumor-Caused-Death set INCIDENTAL
IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some) Note:

Tumor Type:

Symbols, ^, +, or \* represents that the P-value is in the range of [0, 0.005), [0.005, 0.025), or [0.025, 0.05)

RGAN	ORGAN	TUMOR	TUMOR	TUMOR	TIME		P VALUE		
AME	CODE	NAME	CODE	TYPE	INTERVAL	ROW TABLE	EXACT PERMU	ASYMP- TOTIC	CONTINU
DRENAL	CO(4401	) ADENOMA,	TYPE (440118	) IN	IN 79-94	1 .	1.000	0.800	0.800
		<b>7</b> 7			IN 79-94	2		0.000	0.800
DRENAI.	ME (4402	/ DRECCABO	rate: 1%	in CTL	- Total	1.			
a guide		THEOCHRO	10CYT (440201	) 1N		<u>1</u>	1.000	0.795	0.796
		Tumor	rate: 1%	ייי רייי	IN 95-96 - Total	2			
YSTEMIC	N(4500	) MALIGNAN	LYM (450001	) MX	TN 0-52	2 1	0.177		
					IN 0-52	2	0.177	0.177	0.176
					IN 53-78	ī			
					IN 53-78	2			
					IN 79-94	1		خندت	
					IN 79-94	2			
					IN 95-96-	1/ 2/ 1			
					IN 95-96	2			
					FA 28 FA 28	$\frac{1}{2}$			
					FA 30	1			
					FA 30	2	<del></del>		
					FA 33	1			
					FA 33	2			
					FA 39	# 그렇			
					FA 39	2			
					FA 43	1			
					FA 43	2			
					FA 50 FA 50	1 2			
					FA 52	1			
					FA 52	2			
					FA 54	1			
					FA 54	2			
					FA 61	1			
					FA 61	2			
					FA 62	1			
					FA 62	2			
					FA 63	1			
					FA 63 FA 65	2			
					A 65	2			
					A 66	1			
					A 66	2			
					A 68	1			
					. 69	i <b>2</b>			
					A 69	<b>1</b> 10			
					A 69	2			
					A 70	1			
					A 70	2			
e -	7 - 10	ver)			'A 73				

Analysis of Carcinogenic Potential in Female Mouse Test of Carcinogenic rotential in remain mouse
Test of Dose-Response (Tumor) Positive Linear Trend
Run Date & Time: March 7, 1997 (14:52
Source: c:\amcuse\xrod.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

For missing Tumor-Caused-Death set INCIDENTAL Note:

Tumor Type: IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some) Symbols, ^, +, or \* represents that the P-value is in the range of [0, 0.005), [0.005, 0.025), or [0.025, 0.05)

	ORGAN	ORGAN	TUMOR	TUMOR	<b></b>			P VALU	ES	
	NAME	CODE	NAME	CODE	TUMOR TYPE	INTERVAL	. ROW TABLE	EXACT PERMU	ASYMP- TOTIC	CONTINU CORRECT
						IN 53-78				
						IN 53-78 IN 79-94	The second secon			
						IN 79-94				
						IN 95-96				
						IN 95-96	2			
			Tumor	rate: 1%	in CTL	- Total	11. jedin <u>a</u> je			
	SYSTEMIC	N (4500	)MYELOID I	EUKE (45000	)4 ) MX			0.488	0.467	0.467
						IN 95-96				0.40
						FA 67	1			
						FA 67 FA 74	2			
						FA 74	1 2			
						FA 89	$/\frac{2}{1}$			
						FA 89	/ 2			
			Tumor	rate: 2%	in CTL	- Total	/ =			
	SPLEEN	(4600	HISTIOCYT	IC S(04001	5 ) MX	FA 57	1	0.597	0.575	0.575
						FA 57	2			
						FA 95	1			
			Tumor	rate: 1%	in CTI	FA 95	2			
	SFLEEN	(4600	) HEMANGIOS	ARCO (18000	3 ) MY	- loral	1			
<u>(</u>						FA 82	2	0.371	0.301	0.301
			Tumor	rate: <1%	in CTL	- Total				
	THYMUS	(5000	) HISTIOCYT	IC S(04001	5 ) MX	IN 53-78	1	0.556	0.549	C.549
						IN 53-78	2	0.000	0.545	0.549
						FA 95	1			
			77.14.24			FA 95	2			
	THYMUS	(5000	) THYMOMA (1	rate: 1%	IN CIL	- Total	18 17 <del>1</del> 2 18 18 18 18 18 18 18 18 18 18 18 18 18 18 1			
			, , , , , , , , , , , , , , , , , , , ,	D) (30001.		IN 53-78	1	0.419	0.535	0.536
						IN 95-96	2 1			
						IN 95-96	2			
			Tumor	rate: <1%	in CTL	- Total				
	LYMPH NO	DE (5100	)HISTIOCYT	IC S(04001	5 ) MX	FA 95	1	0.348	0.294	0.294
						FA 95	2			
	LYMPH NO	DF (5100	TUMOR	rate: <1%	in CTL	- Total				
	5111111 NO.	22(3100	) HEMANGIOMA	1 (0(16021)			1	0.250	0.054	0.054
			Tumor	rate: <1%	ir cri	IN 0-52	2			
	LYMPH NO		METASTATIO	CA(510016	TN TN	- 10181 TN 95-64				
	Fage -	9 - (0	Over)			55 - 50		1.000	0.796	C.796

Analysis of Carcinogenic Fotential in Female Mouse
Test of Dose-Response (Tumor) Positive Linear Trend
Run Date & Time: March 7, 1997 (14:52)
Source: c:\amouse\xrod.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)
For missing Tumor-Caused-Death set INCIDENTAL
IN: Incidental (Possatal) to all Factoria to all Maximum March 1885)

Note:

Tumor Type: IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some) Symbols, ^, +, or \* represents that the P-value is in the range of [0, 0.005), [0.005, 0.025), or [0.025, 0.05)

ORGAN	ORGAN	TUMOR							P VALU	£S .	
NAME	CODE	NAME	TUMOR CODE	TUMOR					EXACT	ASYMP-	CONTINU
		MAILE	CODE	TYPE	INT	ERVAL	ROW	TABLE	PERMU	TOTIC	CORRECT
					TN	95-96	2				
		Tumor	rate: 1%	in CTL			_				
MESENT.	LY (5104	HISTIOCYT	IC S(0400)	.5 ) MX	FA	95	1		0.040		
					FA		2		0.348	0.294	0.294
		Tumor	rate: <1%	in CTL	_	Total					
MESENT.	LY (5104	) HEMANGIOM	A (C(1602)	2 ) IN	IN .	79-94	1		0.889	0.874	0.874
						79-94	2		0.669	0.674	0.674
					IN S	95-96	1				
					IN S	95-96	2				
UNDDDDT	DN: 45466	Tumor	rate: 1%	in CTL	- 1	<b>rotal</b>	-				
HAKDEKI	AN (5400	) ADENOCARC	INOM (16011	0 - MX			1		0.060	0.052	0.052
						53-78	2				
		<b>4</b> 5					/ 1				
						79-94	2				
						95-96 /					
					IN S	95-96/	2				
HARDERT	AN (5400	I UMOF 1	rate: <1%	in CTL	- 1	otal	7				
III II CDEICE.	-MV (5400	) ADENOMA (	-) (16011				1		0.531	0.598	0.598
						3-78	2				
						9-94	1				
						9-94	2				
						95-96	1				
		Tumor	ate: 1%	in CTI	TN 3	95-96	2				
MAMMARY	GL(5600	) ADENOCARCI	NOM (16011	O NWY	TNI E	Otal	- 1		11 12 12 14		
						3-78	2		0.985	0.957	0.957
						9-94	1				
						9-94	2				
						5-96	î l				
						5-96	2				
					FA 8	200	ī				
					FA 8		2				
		Tumor r	ate: 5%	in CTL	- T	otal	<u> </u>				
SKIN/SUE	3CU (5700	MALIGNANT	SCH (01001.	2 ) MX	IN 9	5-96	1		0.191	0.137	0.137
					IN 9	5-96	2			0.13	0.13/
					FA 8	2	1				
					FA 8	2	2				
					FA B	6	1				
					FA 8	6	2				
CVTNICE	A	Tumor r	ate: <1%	in CTL	- T	ctal	_				
SKIN/SUE	(2700	) HEMANGIOSA	RCO(18000)				1		1.000	0.900	0.800
E	10				IN 7	9-94	2				
Fage -	10 - (:	Over									

Analysis of Carcinogenic Potential in Female Mouse Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: March 7, 1997 (14:52) Source: c:\amouse\xrod.txt

Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500) Note: For missing Tumor-Caused-Death set INCIDENTAL

Tumor Type: IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some) Symbols, ^, +, or \* represents that the P-value is in

the range of [0, 0.005), [0.005, 0.025), or [0.025, 0.05)

ORGAN NAME	ORGAN CODE	TUMOR NAME	TUMOR TUMOR CODE TYPE		ME FERVAL	ROI	W TABLE	P VALUE EXACT PERMU	S ASYMP- TOTIC	CONTINU CORRECT
SKIN/SU	BCU (5700	Tumor r )SQUAMOUS C	ate: 1% in CTI ELL(570001 ) MX	IN IN FA	95-96 95-96 77	- 1 2 1		0.659	0.745	0.745
SKIN/SU	BCU (5700	) KERATOACAN'	ate: <1% in CTL THO(570020 ) IN	IN IN	79-94 79-94	2 1 2		1.000	0.800	0.800
EARS	(6600	Tumor ra )MALIGNANT S	ate: 1% in CTL SCH(010012 ) MX	IN	Total 95-96 95-96	1 2		1.000	0.796	0.796
BODY CA	VIT(6800	Tumor ra )HISTIOCYTIC	te: 1% in CTL CS(040015 ) MX		Total 57	_ / 1		1.000	0.794	::0.794
TAIL	(7400	Tumor ra )MALIGNANT S		- IN	Total / 95-96	1		1.000 _	0.796	_0.796
Page -	11 - (1	Tumor ra End of File)	te: 1% in CTL		95-96 Total	2				

## Analysis of dose-response trend in mouse for hemangioma -hemangiosarcoma combined

Analysis of Carcinogenic Potential in Male Mouse Test of Dose-Response (Tumor) Positive Linear Trend Ted Guo, PH.D, CDER/FDA Run Date & Time: March 18, 1997 (16:25)

Note:

Source: c:\\_data\cbmice.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

For missing Tumor-Caused-Death set INCIDENTAL

ORGAN ORGAN							P VALUES			
VAME	CODE	TUMOR NAME	TUMOR CODE	TUMOR TYPE		ROW	TABLE	EXACT PERMU		CONTING
DRGANS	WITH HEMANG*	HEMANGIOM	+HEMANGIO-	MX	IN 53-78	1				
			SARCOMA		IN 53-78	2		0.225	0.232	0.232
					IN 79-91	ī				
					IN 79-91	2				
					IN 92-104	1				
					IN 92-104	2				
					IN 105m 05	1				
					IN 105-105					
					FA 82 / FA 82 /	1 2				
					FA 83	1				<del></del>
					FA 83	2				
					FA 85	1				
						2				
						1				
						2				
						1				
						2				
						2				
						1				
					FA 104	2				
11ED 0		Tumor r	ate: 10% i	n CTL	m_4_1	_				
EK O	RGAN (OTHER )	OTHER TUMO	R (OTHER	) MX	IN 0-52	1		0.889	0.599	0.887
						2				0.00
						1				
						2				
					and the same of th	1				
						2 1				
						2				
					N 105-105					
					N 105-105					
					and a first control of the first terms.	1				
				1		2				
						1				
						2				
					A 55					
					A 55					
					'A 62 1 'A 62 2					
					'A 62 2 'A 65 1	<u> </u>				
					A 65 2					
					A 66 1					
					A 66 2					
					A 70 1					
					A 70 2					
je -	1 - (Over			L.	A 71 1					

ASYMP- CONTINU TOTIC CORRECT

(Continued)

Note:

Analysis of Carcinogenic Potential in Male Mouse Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: March 18, 1997 (16:25)

Source: c:\\_data\cbmice.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

For missing Tumor-Caused-Death set INCIDENTAL

ORGAN NAME	ORGAN CODE		TUMOR TUM CODE TY	OR TIME PE INTERVAL	ROW TABLE	P VALUES EXACT F PERMU T
				FA 71	2 .	
				FA 72	## <b>1</b> #	
				FA 72	2.1	
				FA 74		
				FA 74 FA 78	2	
				FA 78	1 2	
				FA 80		
				FA 80	2	
				FA 81	1	
				FA 81	2	
				FA 82		
				FA 82	<b>2</b>	
				FA 83 FA 83	<b>1</b>	
				FA 84	/ 2 1	
				FA 84 /	/ <b>2</b>	
				FA 85	Transfer in the second	
				FA 85	2	
				FA 88		
				FA 88	2 2 W	
				FA 89		
				FA 89	2	
				FA 90		
				FA 90 FA 91	2 1	
				FA 91	2	
				FA 93		
				FA 93	2	
				FA 94		
				FA 94	<b>32</b> 33	
				FA 96		
				FA 96	2	
				FA 98		
				FA 98 FA 99	2 1	
				FA 99	2	
				FA 100	# <b>.1</b>	
				FA 100		
				FA 101	2 1 2	
				FA 101	2	64 E34
				FA 102		
				FA 102	H2 11 11 11 11 11 11 11 11 11 11 11 11 11	
				FA 103		
				FA 103	<b>.</b> 2	
				FA 104 FA 104	1 2	
		Tumor rate	: 87% in CTI			
ge 🗕	2 - (Enc	of File)				

Analysis of Carcinogenic Potential in Female Mouse Test of Dose-Response (Tumor) Positive Linear Trend
Ted Guc, FH.D. CDER/FDA
Run Date & Time: March 18, 1997 (16:29)

Note:

Source: c:\\_data\cbmice.txt

Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

For missing Tumor-Caused-Death set INCIDENTAL

ORGAN	ORGAN	TUMOR	MI DAOD				P VALU	ES	
NAME	CODE	NAME	TUMOR CODE	TUMOR TYPE	TIME INTERVAL	ROW TABLE	EXACT PERMU	ASYMP- TOTIC	CONTINU
DRGANS	WITH HEMANG*	HEMANGIOMA	+HEMANGIO- SARCOMA		IN 0-52 IN 0-52 IN 79-91 IN 79-91 IN 92-104 IN 92-104 FA 69 FA 69 FA 82 FA 82	1 2 1 2 1 2 1 2 2 1 2 2 2 2 2 2 2 2 2 2	0.331	0.336	0.336
					FA 85 FA 85 FA 91	1 2 /1 /2 1			
THER O	RGANS (OTHER	Tumor r	ate: 6% i	n CTL MX	FA 94 / - Total/ IN 0-52	<u>2</u> 1	0.188	0.189	
					IN 0-52 IN 53-78 IN 53-78 IN 79-91	2 1 2 1		0.189	0.190
					IN 79-91 IN 79-91 IN 92-104 IN 92-104	1 2 1 2			
					FA 28 FA 28 FA 30 FA 30	1 2 1 2			
					FA 33 FA 33 FA 39	1 2 1			
					FA 39 FA 43 FA 43	2 1 2			
					FA 50 FA 50 FA 52 FA 52	1			
					FA 54 FA 54 FA 54 FA 57	2 1 2 1			
					FA 57 FA 61 FA 61	2 1 2			
					TA 62 TA 62 TA 63	1 2 1			

ASYMF- CONTINU CORRECT

TOTIC

(Continued)

Analysis of Carcinogenic Potential in Female Mcuse Test of Dose-Response (Tumor) Fositive Linear Trend Run Date & Time: March 18, 1997 (16:29)

Note:

Source: c:\\_data\cbmice.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500) For missing Tumor-Caused-Death set INCIDENTAL

IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some) Symbols, ^ and + indicate that p-values are <0.005 and <0.025 respectively

ORGAN NAME	ORGAN CODE	TUMOR NAME	TUMOR CODE	TUMOR TIME TYPE INTERVAL	ROW TABLE	P VALUE EXACT PERMU
				FA 63	2 -	
				FA 65	1	
				FA 65 FA 66	2 1	
				FA 66	2	
				FA 67	i i i	
				FA 67	2	
				FA 68	1	
				FA 68 FA 69	2	
				FA 69	1 2	
				FA 70	1	
				FA 70	$\frac{1}{2}$	
				FA 72	/ <b>1</b>	
				FA 72	/ 2	
				FA 73 / FA 73 /	1	
				FA 74	2	
				FA 74	2	
				FA 75	ī	
				FA 75	2	
				FA 76	<b>1</b>	
				FA 76 FA 77	2	
				FA 77	1 2	
				FA 78	î	
				FA 78	2	
				FA 79	1	
				FA 79	2	
				FA 80	1	
				FA 80 FA 81	2	
				FA 81	2	
				FA 82	ī	
				FA 82	2	
				FA 83	1	
				FA 83 FA 84	2	
				FA 84	1 2	
				FA 85	î	
				FA 85	2	
				FA 86	1	
				FA 86	2	
				FA 87	1	
				FA 67 FA 66	2 1	
				FA 88	2	
				FA 89	î	
ade -	2 - IOve			FA 89	2	

Fage - 2 - (Over)

Note:

Analysis of Carcinogenic Potential in Female Mouse Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: March 18, 1997 (16:29)

Source: c:\\_data\cbmice.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

For missing Tumor-Caused-Death set INCIDENTAL
IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some)
Symbols, ^ and + indicate that p-values are <0.005 and <0.025 respectively

ORGAN NAME	ORGAN CODE	TUMOR NAME	TUMOR CODE	TUMOR TYPE	TIME INTERVAL	ROW TABLE	P VALUES EXACT ASYMP- CONTINU PERMU TOTIC CORRECT
					FA 90	<b>1</b> -	
					FA 90	2	
					FA 91		
					FA 91	2	
					FA 92	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
					FA 92	2	
					FA 93	1	
					FA 93	2	
					FA 94	1 1 ii	
					FA 94	2	
					FA 95	로 <b>1</b> 분부	
					FA 95	2	
Page -	3 - (E	Tumor r nd of File)	ate: 90%	in CTL	- Total	<u>/</u>	
					/		

## Analysis of dose-response trend in mouse for hemangioma -hemangiosarcoma separately

Analysis of Carcinogenic Potential in Male Mouse Test of Dose-Response (Tumor) Positive Linear Trend Ted Guo, PH.D, CDER/FDA Run Date & Time: March 19, 1997 (8:34)

Note:

Source: c:\\_data\hemice.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

For missing Tumor-Caused-Death set INCIDENTAL

ORGAN	ORGAN	TUMOR	TUMOR	TUMOR	TIME			P VALU		
NAME	CODE	NAME	CODE	TYPE	INTERVAL	ROW	TABLE	EXACT PERMU	ASYMP- TOTIC	CONTI
ORGAN	WITH (ORG/160	2) HEMANGIOMA	(C(160212	) IN	IN 53-78	1		0.420		
					IN 53-78	2		0.420	0.440	0.440
					IN 92-104	1				
					IN 92-104					
					IN 105-105	1				
		<b>77</b>			IN 105-105	2				
ORGAN	WITH LORGALED	Tumor ra HEMANGIOSAR	Te: 4%	in CTL	- Total /	-				
		o / MLM MIGIOSAR	(CO(180003	) MX	IN 79-91/	1		0.199	0.199	0.199
					IN 79-91/	2				0.233
					IN 92-104	1				
					IN 92-104	2				
					IN 105-105 IN 105-105	1				
					FA 82					
					FA 82	1 2				
					FA 83	1				
					FA 83	2				
					FA 85	ī				
						2				
						ī				
						2				
					FA 96	1				
						2				
						1				
						2				
						1				
		Tumor rat	D 68			2				
THER C	ORGAN (OTHER	OTHER TUMOR	COTHER	I CIT	- Total	-				
			, oznan			j		0.889	0.888	0.887
						2				
						1 2				
						1				
						2				
						i				
						2				
				1	N 105-105	1				
				1	N 105-105 2	2				
					A 41 ]	1				
				F	A 41 2	2				
					A 52 ]	l				
					A 52 2	2				
				F	A 55 1					
				F F	A 55 1 A 55 2	) 2				
				F F	A 55 1 A 55 2 A 62 1	: 2				
				F F F F	A 55 1 A 55 2	<b>.</b>				

Analysis of Carcinogenic Potential in Male Mouse Test of Dose-Response (Tumor) Positive Linear Trend

Note:

Run Date & Time: March 19, 1997 (8:34)
Source: c:\\_data\hemice.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500) For missing Tumor-Caused-Death set INCIDENTAL

ORGAN	ORGAN	TUMOR	TUMOR	TUMOR TIME		P VALUES	\$	
NAME	CODE	NAME	CODE	TYPE INTERVAL	ROW TABLE	EXACT PERMU	ASYMP- TOTIC	CONTINU CORRECT
				FA 65	2 -			
				FA 66	19: <b>1</b> : h			
				FA 66 FA 70	2			
				FA 70	1 2			
				FA 71	1 1			
				FA 71	2			
				FA 72 FA 72	1 2			
				FA 74	i			
				FA 74	2			
				FA 78 FA 78	1			
				FA 80	/2 /1			
				FA 80	/ 2			
				FA 81 /	1 2			
				FA 81 / FA 82	1			
				FA 82	2			
				FA 83	1			
				FA 83 FA 84	2			
				FA 84	1 2			
				FA 85	1			
				FA 85	2			
				FA 68 FA 88	1 2			
				FA 89	Ī			
				FA 89	2			
				FA 90 FA 90	1 2			
				FA 91	i			
				FA 91	2			
				FA 93 FA 93	1 2			
				FA 94	1			
				FA 94	2			
				FA 96	1			
				FA 96 FA 98	1 2 1 2			
				FA 98	2			
				FA 99	1			
				FA 99 FA 100	2			
				FA 100 FA 100	1 2			
				FA 101	11			
					2			
					1 2			
Page -	2 - (Ove	r)						

Analysis of Carcinogenic Potential in Male Mouse Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: March 19, 1997 (8:34)

Note:

Source: c:\\_data\hemice.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

For missing Tumor-Caused-Death set INCIDENTAL

IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some) Symbols, ^ and + indicate that p-values are <0.005 and <0.025 respectively

ORGAN NAME	ORGAN CODE	TUMOR NAME	and the second state of the second se	MOR TI			P VALUES	202000000000000000000000000000000000000	CONTINU
			CODE TY	YPE IN	TERVAL ROW	TABLE			CORRECT
					103 1 103 2				
					103 2 104 1				
		Tumor ra	te: 87% in C	FA	104 2 Total -				
Page -	3 - (End o	f File)							

Analysis of Carcinogenic Potential in Temale Mouse Analysis of Carcinogenic Potential in remaie Mouse
Test of Dose-Response (Tumor) Positive Linear Trend
Ted Guo, PH.D, CDER/FDA
Run Date & Time: March 19, 1997 (8:40)
Source: c:\\_data\hemice.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

Note:

For missing Tumor-Caused-Death set INCIDENTAL

ORGAN NAME	ORGAN CODE	TUMOR NAME	TUMOR CODE	TUMOR TYPE	TIME INTERVAL	ROW	TABLE	P VALUE EXACT PERMU	S ASYMP- TOTIC	CONTINU CORRECT
ORGAN	WITH (ORG/16	02)HEMANGIOMA	(C(160212	) IN	IN 0-52	1				
					IN 0-52	2	•	0.283	0.278	0.278
					IN 79-91	1				
					IN 79-91	2				
					IN 92-104	1				
					IN 92-104	2				
DCNN 1		Tumor ra	te: 2% ;	n CTL	- Total	_				
KGAN I	MITH (OKG) 18	00)HEMANGIOSAR	CO(180003	) MX	IN 79-91	1		0.481	0.494	0.494
					IN 79-91	2			0.434	0.494
					IN 92-104	1				
					IN 92-104	2				
					FA 69	1				
					FA 69	2				
					FA 82 🖳 /	1				
					FA 82 /	2				
					FA 85 /	1				
					FA_85/	2				
					FA 91	1				
					FA 91	2				
					FA 94	1				
		Tumor ra	e 48 4	D C77	FA 94 - Total	2				
THER C	ORGA (OTHER	)OTHER TUMOR		1 MY	IN 0-52	- 1				
			(01115)(		IN 0-52	2		0.188	0.189	0.190
					IN 53-78	1				
					IN 53-78	2				
					IN 79-91	1				
					IN 79-91	2				
						ì				
						2				
						í				
						2				
						ī				
						2				
						1				
				I		2				
				ľ	A 39	1				
				F	A 39	2				
				F	A 43	1				
						2				
						1				
						2				
						1				
						2				
						l				
					A 54 ; A 57 ;	2				

ASYMP- CONTINU TOTIC CORRECT

(Continued)

Analysis of Carcinogenic Potential in Female Mouse Analysis of Carcinogenic Potential in Female Mouse
Test of Dose-Response (Tumor) Positive Linear Trend
Run Date & Time: March 19, 1997 (8:40)
Source: C:\\_data\hemice.txt

Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)
For missing Tumor-Caused-Death set INCIDENTAL
IN: Incidental (Defeated) to all the set INCIDENTAL

Note:

IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some) Symbols, ^ and + indicate that p-values are <0.005 and <0.025 respectively.

ORGAN NAME	ORGAN CODE	TUMOR NAME	TUMOR CODE	TUMOR TIME TYPE INTERVAL	L ROW TABLE	P VAL EXACT PERMU
				FA 57	<b>.</b>	231410
				FA 61	i i	
				FA 61	2	
				FA 62	1	
				FA 62	2	
				FA 63 FA 63	1	
				FA 65	2 1	
				FA 65	2	
				FA 66	Ī	-1311
				FA 66	2	
				FA 67	3 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
				FA 67	/ 2	
				FA 68	/ 1	
				FA 68 FA 69	/ 2	
				FA 69	/ 2	
<u> </u>				FA 70	i	
				FA 70	$\overline{2}$	
				FA 72	1	
				FA 72	2	
				FA 73		
				FA 73 FA 74	2.11.1 1	
				FA 74	2	
				FA 75	1 . <b>.</b>	
				FA 75	2	
				FA 76		
				FA 76	2	
				FA 77 FA 77		
				FA 78	2 1	
				FA 78	2	
				FA 79		
				FA 79	2	
				FA 80		
				FA 80	2	
				FA 81 FA 81	1	
				FA 82	2	
				FA 82	2	
				FA 83	<b>1</b>	
				FA 83	2	
				FA 84	1981 <b>프</b> 레이션:	
				FA 84	2	
				FA 85 FA 85	1 2	
				FA 86	í	
				FA 86	2	
age -	2 - (Ove	r)				

Analysis of Carcinogenic Fotential in Female Mouse Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: March 19, 1997 (8:40)

Note:

Source: c:\\_data\hemice.txt

Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

For missing Tumor-Caused-Death set INCIDENTAL

IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some)

Symbols, ^ and + indicate that p-values are <0.005 and <0.025 respectively

ORGAN NAME	ORGAN CODE	TUMOR NAME	TUMOR CODE	TUMOR TYPE	TIME INTERVA	L ROW	TABLE		TINU RECT
					FA 87	1			
					FA 87	2			
					FA 88	1			
					FA 88	2			
					FA 89	1			
					FA 89	2			
					FA 90	1			
					FA 90	2		사용하다 하다 하다 하다 하다 하다 하다 하다.	
					FA 91	$\bar{1}$			
					FA 91	2			
					FA 92	i			
					FA 92	2		물 등 하다 가장 그 것 같은 말이 되었다.	
					FA 93	1			
					FA 93	/2			
					FA 94	/ ī			
					FA 94	/ 2			
					FA 95	/ ī			
			ورون المسار المستحد المستحد الرون المسار المستحد المستحد		A 95	2			
Page -	3 - (En	Tumor r d of File)	ate: 90%	and the state of t	- Total				

## References

3

Lin et al (1994). "Statistical Review and Evaluation of Animal Tumorigenicity Studies." <u>Statistics in the Pharmaceutical Industry</u>. Marcel Dekker, Inc. pp. 19-57.

Thomas et al (1976). "Trend and Homogeneity Analyses of Proportions and Life Table Data." Computers and Biomedical Research. pp. 373-81.

Peto et al (1980). "Guidelines for Simple, Sensitive Significance Tests for Carcinogenic Effects in Long-Term Animal Experiments. In Long-Term and Short-Term Screening Assays for Carcinogens: An Critical Appraisal, International Agency for Research on Cancer, Lyon, France. <u>IARC Monographs Supplement 2</u>. pp. 311-426.

Haseman, J. K. (1983). "A re-examination of false-positive rates for carcinogenesis studies." / Fundamental and Applied Toxicology 3, pp. 334-9.

Haseman, J. K. (1984). "Issues in carcinogenicity testing: Dose selection." <u>Fundamental and Applied Toxicology</u>, Vol. 5. pp.

Analysis of Carcinogenic Potential in Male Rat Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: February 26, 1997 (16:10) Source: c:\arat\xrod.txt

Dose Levels Included: CTRL1 CTRL2 LOW MEDIUM HIGH (0 0 150 500 1000) For missing Tumor-Caused-Death set INCIDENTAL

Tumor Type: IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some)

Symbols [^---] [-%--] [--+-] [---+-] ^ % + +

Represent 0<P<0.005 0.005<=P<0.01 0.01<=P<0.025 0.025<=P<0.05 P<.005 P<.01 P<.025 P<.05

								P VALUE	:s	
ORGAN NAME	ORGAN CODE		TUMOR CODE	TUMOR				EXACT	ASYMP-	CONTINU
MAPIE.	CODE	NAME	CODE	TYPE	INTERVA	L R	OW TABLE	PERMU	TOTIC	CORRECT
					IN 105-	106 2				
					FA 52	1				
					FA 52	2				
					FA 78	1				
					FA 78	2				
					FA 102 FA 102	1 2				
		Tumor i	ate: 3%	in CTL						
HENOT VIVI	211074500									
HEMOLYMI	PHO (4500	HISTIOCYTI	C S(45000)	3 ) FA	FA 65	1 2		0.390	0.256	0.256
		Tumor	ate: _1%	in CTL						
SPLEEN	(4600	VALCETOCAM				/ .				
SFLEEN	14800	HISTIOCYTI	C 2(01001)	J ) MX	FA 65	/ 1		0.193	0.037*	0.037*
		Tumor i	ate: <1%	in CTL				<u> ar stalen en jaar al en</u> Laar en <u>en tale</u> en se	[*]	[*]
SPLEEN	(4600	) HEMANGIOSA	RC01460014	1 ) TN	TN 105-	106 1		1.000	0.791	0.792
					IN 105-			1.000	0.791	0.792
		Tumor r	ate: 1%	in CTL						
SPLEEN	(4600	) SARCOMA, N	OT (460016	5 ) MX	TN 105-	106.1		1.000	0.791	0.702
					IN 105-			1.000	0.791	0.792
		Tumor r	ate: 1%	in CTL	- Tota	l -				
SPLEEN	(4600	) HEMANGIOMA	(C(460018	3 ) MX	IN 105-	106 1		0.173	0.030*	0.030*
					IN 105-1	106 2			0.050	0.050
		Tumer r	ate: <1%	in CTL	- Tota	1 -			[+)	[+]
BONE MAR	RO(4700	) HISTIOCYTI	C S(010010	) MX	FA 65	1		0.193	0.037*	0.037*
					FA 65	2		0.155	0.03	0.037
		Tumor	ate: <1%	in CTL	- Total	i -			[+]	[*]
LYMPH NO	DE (5100	) HISTIOCYTI	C S(010010	) MX	IN 0-78	1		0.667	0.240	0.241
					IN 0-78	2				
		Tumor r	ate: <14	in CTL	- Total		 			
MESENT.	LY(5104	) HISTIOCYTI	C S(010010	) MX	IN 0-78	1		0.667	0.240	0.241
			ila kateari		IN 0-78	2				
		Tumor r	ate: <1+	in CTL	- Total	L -				
MESENT.	LY (5104	) HEMANGIOSA	RC0(460014	) IN	IN 94-10	04 1		0.906	0.837	0.937
					IN 94-10					
					IN 105-1					
		Tumer r	ate: 1%	in CTL	IN 105-1					
MESENT.	LY (5104	HEMANGIOMA	(C(460019					0.729	0.727	0.727
Page -	5 - 6	Over)			IN 94-10	)4 2				

Analysis of Carcinogenic Potential in Male Rat Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: February 26, 1997 (16:10) Source: c:\arat\xrod.txt

Dose Levels Included: CTRL1 CTRL2 LOW MEDIUM HIGH (0 0 150 500 1000) For missing Tumor-Caused-Death set INCIDENTAL Note: 

	000000							P VALU	23	
ORGAN NAME	ORGAN CODE	TUMOR NAME	TUMOR CODE	TUMOR TYPE	TIME INTERVAL	ROW	TABLE	EXACT PERMU		CONTING CORREC
					IN 105-10	6 1				
					IN 105-10	T				
					FA 97	î				
					FA 97	2				
		Tumor	rate: 18%	in CTL	- Total	<b>É</b>				
MANDIBUL	. (5108	) HISTIOCYT	IC S(01001	0 ) MY	TN 0-78					
				0 / 11/		2 .		0.667	0.240	0.241
		Tumor	rate: <1%	in CTL	- Total					
HARDERIA	N (5400	) HISTIOCYT	TC 8/01001	0 ) W	TV 0 70					
en Richarden		////	10 3(01001	O ) MX		1		0.667	0.240	0.241
		<b></b>			IN 0-78	/ 2				
		Tumor	rate: <1%	in CTL	- Total	/ -				
HARDERIAN (5	N (5400	) ADENOCARC	INOM (54001	1 ) IN	IN 105-10	6 1		0.378	0.296	0.206
					IN 105-10	6 2		0.370	0.230	0.296
		Tumor	rate: <1%	in CTL	- Total					
EXORBITA:	L (5520	) HISTIOCYT	IC S(01001	0 ) MX	IN 0-78	1		1.000	0.930	0.000
					IN 0-78	2		1.000	0.930	0.930
		Tumor	rate: 1%	in CTL	- Total					
AMMARY (	GL(5600	) HISTIOCYT:	C 5/01001	0 ) MV	TN 0.70	1				
		,			IN 0-78			0.667	0.240	0.241
		Tumor	rate: <1%	4 - 007	IN 0-78	2				
		1 dmo1 1	are: <14	in CIL	- Total	-				
SKIN	(5700	) HISTIOCYT	C S(01001	0 1 MX	IN 0-78	1		0 667	0 340	0.041
			1.000.001.00		IN 0-78	2		0.007	0.240	0.241
		Tumor :	ate: <1%	in CTL	- Total	_				
SKIN	(5700	) SQUAMOUS (	FIT (09003)	9 1 FA	EN 00					
						1		D.648	0.721	0.721
					FA 99	2				
					FA 103	1				
		Tumor r	ate: <1%	in CTI	FA 103	2				
SKIN	(5700	) MALIGNANT	SCH (340007	7 ) FA	FA 76	1		0.171	2.154	0.154
					FA 76	2				0.101
					FA 102	.1				
					FA 102	2				
		Tumer r	ate: <1%	in CTL	- Total	-				
KIN	(5700	) ADENOMA (C	1 (430006	, TN	TN 105-106					
					IN 105-106			1.000	1.791	0.792
		- Tumor r	ate: 1%	in CTL	- Total	1				
KIN	(5700									
/. L _ 1 \	(3/00	) HEMANGIOSA	KCU (460014					0.546	0.658	0.658
				التستوال الما	IN 105-106	3 €				
		Tumor r	are: <14	in CTL	- Total	-				
								and the second s		

Analysis of Carcinogenic Potential in Male Rat Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: February 26, 1997 (16:10)

Source: c:\arat\xrod.txt

Dose Levels Included: CTRL1 CTRL2 LOW MEDIUM HIGH (0 0 150 500 1000)

Note: For missing Tumor-Caused-Death set INCIDENTAL

P VALUES ORGAN ORGAN TUMOR TUMOR TIME TUMOR **EXACT** ASYMP-CONTINU NAME CODE NAME CODE TYPE INTERVAL ROW TABLE PERMU TOTIC CORRECT SKIN (5700 )SARCOMA, NOT (460016 ) MX FA 90 1 1.000 0.799 0.799 FA 90 2 Tumor rate: 1% in CTL - Total SKIN (5700 ) HEMANGIOMA (C(460018 ) MX IN 105-106 1 0.378 0.296 0.296 IN 105-106 2 Tumor rate: <1% in CTL - Total SKIN (5700 ) FIBROMA (570010 ) IN IN 105-106 1 0.378 0.296 0.296 IN 105-106 2 Tumor rate: <1% in CTL - Total /-SKIN 15700 )KERATOACANTHO(570011 ) IN IN 94-104/ IN 94-104 1 IN 94-104 2 0.232 0.220 0.220 IN 105-106 1 IN 105-106 2 Tumor rate: 6% in CTL - Total SKIN 15700 ) SQUAMOUS CELL (570012 ) IN IN 79-93 0.248 0.189 0.189 IN 79-93 IN 105-106 1 IN 105-106 2 in CTL - Total Tumor rate: 1% SKIN 15700 )BASAL CELL CA(570016 ) MX IN 105-106 1 0.329 0.290 0.291 IN 105-106 2 FA 64 1 FA 64 2 FA 77 FA 77 FA 90 1 FA 90 2 Tumor rate: 3% in CTL - Total SYTH (5700 )LIPOSARCOMA ((570018 ) FA FA 53 1 0.194 0.037\* 0.038+ FA 53 2 Tumor rate: <1% in CTL - Total [---+] [---+] SKI (570C )BASAL CELL AD(570019 ) IN IN 105-106 1 0.522 0.439 0.440 IN 105-106 2 in CTL - Total Tumor rate: 18 SYIN (5700 )FIBROSARCOMA (570025 ) MX IN 105-106 1 0.449 0.480 0.481 IN 105-106 2 FA 61 FA 61 2 Tumor rate: <1% in CTL - Total TZYMBAL'S GLAN(570031 ) IN IN 79-93 SKIN (5700 0.034\* 0.034\* Fage -7 - (Over)